CLAIMS

1. An isolated antibody, or one of its functional fragments, said antibody or one of its said fragments being capable of binding to the human insulin-like growth factor I receptor IGF-IR and, if necessary, inhibiting the natural attachment of its ligands IGF1 and/or IGF2 and/or capable of specifically inhibiting the tyrosine kinase activity of said IGF-IR receptor, characterized in that it comprises a light chain comprising at least one complementarity determining region CDR chosen from the CDRs of sequence SEQ ID No. 2, 4 or 6, or at least one CDR whose sequence has at least 80% identity after optimum alignment with the sequence SEQ ID No. 2, 4 or 6, or in that it comprises a heavy chain comprising at least one CDR chosen from the CDRs of sequence SEQ ID Nos. 8, 10 and 12, or at least one CDR whose sequence has at least 80% identity after optimum alignment with the sequence SEQ ID No. 8, 10 and 12.

2. The antibody, or one of its functional fragments, as claimed in claim 1, characterized in that it comprises a heavy chain comprising at least one CDR of sequence SEQ ID No. 12 or a sequence having at least 80% identity after optimum alignment with the sequence SEQ ID No. 12.

3. The antibody, or one of its functional fragments, as claimed in claim 1 or 2, characterized in that it comprises a heavy chain comprising at least two of the three CDRs or the three CDRs of sequence SEQ ID Nos. 8, 10 and 12, or at least two of three CDRs or three CDRs of sequence respectively having at least 80% identity after optimum alignment with the sequence SEQ ID No. 8, 10 and 12.

4. The antibody, or one of its functional fragments,

as claimed in one of claims 1 to 3, characterized in that it comprises a light chain comprising at least one CDR chosen from the CDRs of sequence SEQ ID No. 2, 4 or 6, or a CDR whose sequence has at least 80% identity after optimum alignment with the sequence SEQ ID No. 2, 4 or 6.

5. The antibody, or one of its functional fragments, as claimed in one of claims 1 to 4, characterized in that it comprises a light chain comprising at least two of the three CDRs or the three CDRs of sequence SEQ ID Nos. 2, 4 and 6, or at least two of three CDRs or three CDRs of sequence respectively having at least 80% identity after optimum alignment with the sequence SEQ ID No. 2, 4 and 6.

6. The antibody, or one of its functional fragments, as claimed in one of claims 1 to 5, characterized in that it does not attach in a significant manner to the human insulin receptor IR.

7. The antibody as claimed in one of claims 1 to 6, characterized in that said functional fragment is chosen from the fragments Fv, Fab, $F(ab')_2$, Fab', scFv, scFv-Fc and the diabodies, or any fragment whose half-life would have been increased such as pegylated fragments.

8. A murine hybridoma capable of secreting an antibody as claimed in one of claims 1 to 6.

9. The murine hybridoma as claimed in claim 8 deposited at the CNCM, Institut Pasteur, Paris, on September 19, 2001 under the number I-2717.

10. An antibody, or one of its functional fragments, characterized in that said antibody is secreted by the hybridoma as claimed in claim 9.

11. The antibody, or one of its functional fragments, as claimed in one of claims 1 to 7, characterized in that said antibody comprises a light chain of sequence comprising the amino acid sequence SEQ ID No. 54, or a sequence having at least 80% identity after optimum alignment with the sequence SEQ ID No. 54, or/and in that it comprises a heavy chain of sequence comprising the amino acid sequence SEQ ID No. 69, or a sequence having at least 80% identity after optimum alignment with the sequence SEQ ID No. 69.

12. The antibody or one of its functional fragments, as claimed in claim 11, characterized in that said antibody is a chimeric antibody and moreover comprises the light chain and heavy chain constant regions derived from an antibody of a species heterologous to the mouse.

13. The chimeric antibody, or one of its functional fragments, as claimed in claim 12, characterized in that said heterologous species is man.

14. The chimeric antibody, or one of its functional fragments, as claimed in claim 13, characterized in that the light chain and heavy chain constant regions derived from a human antibody are respectively the kappa and gamma-1, gamma-2 or gamma-4 region.

15. The antibody or one of its functional fragments, as claimed in one of claims 1 to 7, characterized in that said antibody is a humanized antibody and comprises a light chain and/or a heavy chain in which the skeleton segments FR1 to FR4 of said light chain and/or heavy chain are respectively derived from skeleton segments FR1 to FR4 of human antibody light chain and/or heavy chain.

16. The humanized antibody, or one of its functional fragments, as claimed in claim 15, characterized in

that said antibody comprises a light chain comprising the amino acid sequence SEQ ID No. 61 or 65, or a sequence having at least 80% identity after optimum alignment with the sequence SEQ ID No. 61 or 65, or/and in that it comprises a heavy chain comprising the amino acid sequence SEQ ID No. 75, 79 or 83, or a sequence having at least 80% identity after optimum alignment with the sequence SEQ ID No. 75, 79 or 83.

17. The humanized antibody, or one of its functional fragments, as claimed in claim 15 or 16, characterized in that said antibody comprises a light chain comprising the amino acid sequence SEQ ID No. 65, and in that it comprises a heavy chain of sequence comprising the amino acid sequence SEQ ID No. 79 or 83, preferably SEQ ID No. 83.

18. An isolated nucleic acid, characterized in that it is chosen from the following nucleic acids:

a) a nucleic acid, DNA or RNA, coding for an antibody, or one of its functional fragments, as claimed in one of claims 1 to 7 and 10 to 17;

b) a complementary nucleic acid of a nucleic acid such as defined in a); and

c) a nucleic acid of at least 18 nucleotides capable of hybridizing under conditions of great stringency with at least one of the CDRs of sequence SEQ ID No. 1, 3, 5, 7, 9 or 11, or with a sequence having at least 80% identity after optimum alignment with the sequence SEQ ID No. 1, 3, 5, 7, 9 or 11.

19. A vector comprising a nucleic acid as claimed in claim 18.

20. A host cell comprising a vector as claimed in claim 19.

21. A transgenic animal with the exception of man comprising at least one cell transformed by a vector as

claimed in claim 19.

22. A process for production of an antibody, or one of its functional fragments, as claimed in one of claims 1 to 7 and 10 to 17, characterized in that it comprises the following stages:

a) culture in a medium and appropriate culture conditions of a cell as claimed in claim 20; and

b) the recovery of said antibodies, or one of their functional fragments, thus produced starting from the culture medium or said cultured cells.

23. An antibody, or one of its functional fragments, capable of being obtained by a process as claimed in claim 22.

24. The antibody, or one of its functional fragments, as claimed in any one of claims 1 to 7, 10 to 17 and 23, characterized in that it is, moreover, capable of attaching specifically to the human epidermal growth factor receptor and/or capable of specifically inhibiting the tyrosine kinase activity of said EGFR receptor.

25. The antibody as claimed in claim 24, characterized in that it consists of a bispecific antibody and in that it comprises a second motif specifically inhibiting the attachment of the EGF to the human epidermal growth factor receptor EGFR and/or specifically inhibiting the tyrosine kinase activity of said EGFR receptor.

26. The antibody as claimed in claim 25, characterized in that it is bivalent or tetravalent.

27. The antibody as claimed in one of claims 25 or 26, characterized in that said second motif is selected from the fragments Fv, Fab, $F(ab')_2$, Fab', Fab'PEG, scFv, scFv-Fc and the diabodies, or any form whose

half-life would have been increased.

28. The antibody as claimed in any one of claims 25 to 27, characterized in that said second anti-EGFR motif is descended from the mouse monoclonal antibody 225, its mouse-man chimeric derivative C225, or a humanized antibody derived from this antibody 225.

29. The antibody, or one of its functional fragments, as claimed in one of claims 1 to 7, 10 to 17 and 23 to 27 as a medicament.

30. A composition comprising by way of active principle a compound consisting of an antibody, or one of its functional fragments, as claimed in one of claims 1 to 7, 10 to 17 and 23 to 29.

31. The composition as claimed in claim 30, characterized in that it comprises a second compound chosen from the compounds capable of specifically inhibiting the attachment of the EGF to the human epidermal growth factor receptor EGFR and/or capable of specifically inhibiting the tyrosine kinase activity of said EGFR receptor.

32. The composition as claimed in claim 31, characterized in that said second compound is chosen from the isolated anti-EGFR antibodies, or their functional fragments, capable of inhibiting by competition the attachment of the EGF to the EGFR.

33. The composition as claimed in claim 32, characterized in that said anti-EGFR antibody is chosen from the monoclonal, chimeric or humanized anti-EGFR antibodies, or their functional fragments.

34. The composition as claimed in either of claims 32 or 33, characterized in that said functional fragments of the anti-EGFR antibody are chosen from the fragments

Fv, Fab, F(ab')$_2$, Fab', scFv-Fc and the diabodies, or any fragment whose half-life would have been increased, like pegylated fragments.

35. The composition as claimed in one of claims 32 to 34, characterized in that said anti-EGFR antibody is the mouse monoclonal antibody 225, its mouse-man chimeric derivative C225, or a humanized antibody derived from this antibody 225.

36. The composition as claimed in any one of claims 30 to 35, characterized in that it comprises, moreover, as a combination product for simultaneous, separate or sequential use, a cytotoxic/cytostatic agent and/or an inhibitor of the tyrosine kinase activity respectively of the receptors for IGF-I and/or for EGF.

37. The composition as claimed in claim 36, characterized in that said cytotoxic/cytostatic agent is chosen from the agents interacting with DNA, the antimetabolites, the topoisomerase I or II inhibitors, or the spindle inhibitor or stabilizer agents or else any agent capable of being used in chemotherapy.

38. The composition as claimed in claim 36 or 37, characterized in that said cytotoxic/cytostatic agent is coupled chemically to at least one of the elements of said composition for simultaneous use.

39. The composition as claimed in claim 37 or 38, characterized in that said cytotoxic/cytostatic agent is chosen from the spindle inhibitor or stabilizer agents, preferably *Vinca* alkaloid, more preferably selected from vinblastine, deoxyvinblastine, vincristine, vindesine, vinorelbine, vinepidine, vinfosiltine, vinzolidine and vinflunine.

40. The composition as claimed in one of claims 36 to 39, characterized in that said inhibitor of the

tyrosine kinase activity respectively of the receptors for IGF-I and/or for EGF is selected from the group consisting of derived natural agents, dianilinophthalimides, pyrazolo- or pyrrolopyridopyrimidines or else quinazilines.

41. The composition as claimed in any one of claims 30 to 40, characterized in that it comprises, moreover, another antibody compound directed against the extracellular domain of the HER2/neu receptor, as a combination product for simultaneous, separate or sequential use intended for the prevention and for the treatment of cancer.

42. The composition as claimed in claim 41, characterized in that said antibody directed against the extramembrane domain of the HER2/neu receptor is Trastuzumab, or one of its functional fragments.

43. The composition as claimed in any one of claims 30 to 42, characterized in that one, at least, of said antibodies, or one of its functional fragments, is conjugated with a cell toxin and/or a radioelement.

44. The composition as claimed in one of claims 30 to 43 as a medicament.

45. The use of an antibody, or one of its functional fragments, as claimed in one of claims 1 to 7, 10 to 17 and 23 to 29 and/or of a composition as claimed in any one of claims 30 to 44 for the preparation of a medicament intended for the prevention or for the treatment of an illness connected with an overexpression and/or an abnormal activation of the IGF-IR and/or EGFR receptor, and/or connected with a hyperactivation of the transduction pathway of the signal mediated by the interaction of IGF1 or IGF2 with IGF-IR and/or of EGF with EGFR.

46. The use as claimed in claim 45, characterized in that the administration of said medicament does not induce or only slightly induces secondary effects connected with inhibition of the insulin receptor IR.

47. The use as claimed in claim 45 or 46 for the preparation of a medicament intended to inhibit the transformation of normal cells into cells with tumoral character, preferably IGF-dependent, especially IGF1- and/or IGF2-dependent and/or EGF-dependent and/or HER2/neu-dependent cells.

48. The use as claimed in any one of claims of 45 to 47 for the preparation of a medicament intended to inhibit the growth and/or the proliferation of tumor cells, preferably IGF-dependent, especially IGF1- and/or IGF2-dependent and/or EGF-dependent and/or HER2/neu-dependent cells.

49. The use as claimed in one of claims of 45 to 48 for the preparation of a medicament intended for the prevention or for the treatment of cancer.

50. The use as claimed in claim 49, characterized in that said cancer is a cancer chosen from prostate cancer, osteosarcomas, lung cancer, breast cancer, endometrial cancer or colon cancer.

51. The use as claimed in one of claims of 45 to 48 for the preparation of a medicament intended for the prevention or for the treatment of psoriasis.

52. A method of *in vitro* diagnosis of illnesses induced by an overexpression or an underexpression of the IGF-IR and/or EGFR receptor starting from a biological sample in which the abnormal presence of IGF-IR and/or EGFR receptor is suspected, characterized in that said biological sample is contacted with an antibody as claimed in one of claims 1 to 7, 10 to 17

and 23 to 29, it being possible for said antibody to be, if necessary, labeled.

53. A kit or set for carrying out a method of diagnosis of illnesses induced by an overexpression or an underexpression of the IGF-IR and/or EGFR receptor or for carrying out a process for the detection and/or the quantification of an overexpression or of an underexpression of the IGF-IR and/or EGFR receptor in a biological sample, preferably an overexpression of said receptor, characterized in that said kit or set comprises the following elements:

a) an antibody, or one of its functional fragments, as claimed in one of claims 1 to 7, 10 to 17 and 23 to 29;

b) optionally, the reagents for the formation of the medium favorable to the immunological reaction;

c) optionally, the reagents allowing the demonstration of IGF-IR/antibody and/or EGFR/antibody complexes produced by the immunological reaction.

54. The use of an antibody, or one of its functional fragments, as claimed in one of claims 1 to 7, 10 to 17 and 23 to 29, for the preparation of a medicament intended for the specific targeting of a biologically active compound to cells expressing or overexpressing the IGF-IR and/or EGFR receptor.